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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/642,409	08/15/2003	Deborah Ann Ansaldi	P1363R1C1	1482

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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/27/2006

Attn: Janet E. Hasak
Genentech, Inc.
1DNA Way
South San Francisco, CA 94080

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/642,409	ANSALDI ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/15/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/06,3/05,8/03,10/0*}.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1 –15 are pending and examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 6, 8-10, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Wan (US 6,177,548; published Jan. 23, 2001; effective filing date 10/14/1997) as evidenced by Li (Li, F. et al, www.bioprocessingjournal.com, September/October, 2005, pages 1-8 in vol. 4(5): page 23).

The claims are drawn to methods for purifying polypeptide monomers from a mixture consisting essentially of polypeptide monomers, and dimers or multimers of the polypeptide monomers or both dimmers and multimers of the polypeptide monomers, where the method comprises: applying he mixture to a cation-exchnge or anion –exchange chromatography resin in a buffer, wherein if the resin is cation-exchange, the pH of the buffer is about 4-7, and wherein if the resin is anion-exchange, the pH of the buffer is about 6-9, wherein the monomer is purified

from the dimers or multimers or both present in the mixture, and wherein the monomer yield is greater than 90%, and recovering the monomer.

Wan discloses a method for purifying monoclonal antibodies from aggregates and other impurities using anion exchange chromatography. Wan defines aggregates as "formed by more than one molecule, or contain partially or completely denatured molecules" (col. 1, lines 18-20). Thus, Wan's aggregates appear to fall within the scope of "multimers", and not the aggregated, denatured molecules discussed in the instant application (page 6, lines 10-13). Wan teaches that aggregates generally carry more charge than the product, when the working pH is close to the product's isoelectric point (in the case of working example uses pH of 8.2). Thus, if the pH is adjusted to close to the isoelectric point of the product, more of the aggregates and other impurities than product will bind to the anion exchange column resulting in purification of the product. Wan discloses a method where the yield of antibody is above 90% (see Tables 1 and 2 "Antibody recovered in collected fraction"). The mixture that is applied to the column is a buffer exchanged antibody fraction, which is the bound fraction from a protein A column (column 2, lines 29-43). The buffer is potassium phosphate, 10mM. The monomeric form elutes before the aggregated form in the potassium phosphate buffer. A sodium chloride buffer is applied that is 1 M. Thus, the gradient is step-wise, with the monomer eluting at 0M sodium salt. Li teaches that protein A chromatography does not remove dimers and aggregates, see page 5). Therefore, Wan's mixture appears to be a mixture consisting essentially of antibody monomers, dimers or multimers. Thus, Wan discloses a method that is the same as that claimed.

3. Claims 1, 5, 6, 8-12, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Jiskoot (Jiskoot, W. et al., Develop. Biol. Standard., Vol. 71: 73-78, 1990) as evidenced by Li (supra).

Jiskoot teaches a method for purifying monoclonal antibodies from bovine IgG present in fetal bovine serum. The method also appears to result in the purification of antibody monomer from antibody multimers (see Table III, page 77 "Gel Permeation pattern (%monomers)"). For antibody WT31, anion exchange chromatography is used, whereas for antibody MN12, cation exchange chromatography is used (page 75). The pH with anion exchange chromatography is 7.5, and pH with cation exchange chromatography is 6.5. The mixture applied to the ion exchange columns is a protein A column eluate that was buffer exchanged. Li teaches that protein A chromatography does not remover dimers and aggregates, see page 5). Thus, Jiskoot's mixture appears to be a mixture of antibody monomers and dimers or multimers. The gradient appears to be stepwise (a wash buffer, followed by an elution buffer (see Table II)). The elution salt is either 0.1M or 0.08M NaCl. Thus, Jiskoot teaches methods that are the same as that claimed.

4. Claims 1, 5, 7, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Bodo (U.S. 5,196,323; published Mar. 23, 1993).

Bodo teaches separation of interferon-alpha monomers from dimers and other oligomers by cation-exchange chromatography (column 10, lines 35-66). The gradient is ammonium acetate, 0-500 mM, and the pH is 4.5-5.0 (see col. 16, lines66-68). The mixture applied to the column is a mixture of monomers and dimers and other oligomers (col. 10, lines lines 14-34).

The yield is 90% (column 6, line 6 – column 7, line 8). Thus, Bodo teaches the methods as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 6, 7, 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary (Chaudhary, V.K. et al., Nature, 339, pages 394-397; cited in IDS) in view of Gagnon (Gagnon, P. et al, Purification Tools for Monoclonal Antibodies, pages 67-86, Validated Biosystems, Inc., Tucson, AZ, 1996; cited in IDS).

Chaudhary teaches a method of purifying the monomeric form of an anti-Tac(fv)-PE40 fusion protein from higher molecular weight aggregates (see page 395, column 1 and Figure 2). The mixture applied to the column in Chaudhary is 100,000g pellet from sonicated spheroplasts. The instant specification defines the "mixture" as containing, which has the same meaning as "comprising", monomers and either dimers or multimers or both (page 5, lines 23-24). Therefore, the transitional phrase "consisting essentially of" appears to have the same meaning as comprising (see MPEP 2111.03, where "consisting essentially of" limits the scope of a claim to the specified materials or steps and those that do not materially affect the basic and novel characteristic(s) of the claimed inventions. For the purposes of searching for and applying prior art, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising").

Chaudhary teaches that fractions 32-33 from an anion exchange column eluate (see lane 4) appears to be free of higher molecular weight dimers or multimers. The elution salt was NaCl, and the gradient was 0 – 500 mM. Therefore, Chaudhary teaches a method that is the same as that claimed.

Chaudhary fails to explicitly teach the yields of the monomer. However, Gagnon teaches that ion exchange chromatography is used to purify proteins and that the mass recovery for

monoclonal antibody is 80-95%, with an average of 90% (see page 64). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Chaudhary to purify the Chaudhary's monomer from dimers and multimers and one would have expected to have a yield of greater than 90% because of the teachings of Gagnon concerning the general knowledge of the ability of ion exchange chromatography to purify monoclonal antibodies.

6. Claims 1, 5, 7, 9, 10, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lynch (Lynch, P., Genetic Engineering News, page 17, November 1, 1997; cited in the IDS) in view of Gagnon (Gagnon, P. et al, Purification Tools for Monoclonal Antibodies, pages 67-86, Validated Biosystems, Inc., Tucson, AZ, 1996; cited in the IDS).

Lynch teaches that a protein A purified cell culture medium was applied to a cation exchange column and eluted by a linear salt gradient, separating the monomer from the aggregated forms of the antibody. Lynch fails to teach the yield of monomer. However, Gagnon teaches that ion exchange chromatography is used to purify proteins and that the mass recovery for monoclonal antibody is 80-95%, with an average of 90% (see page 64). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Lynch to purify the Lynch's monomer from dimers and multimers and one would have expected to have a yield of greater than 90% because of the teachings of Gagnon concerning the general knowledge of the ability of ion exchange chromatography to purify monoclonal antibodies.

7. Claims 1, 2, 4, 6, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gooding (Gooding, K.M. and Schmuck, M.N. Journal of Chromatography, 327: 139-146, 1985) in view of Gagnon (Gagnon, P. et al, Purification Tools for Monoclonal Antibodies, pages 67-86, Validated Biosystems, Inc., Tucson, AZ, 1996; cited in the IDS).

Claims 1, 2, 4, 6 and 9 read on methods for purifying bovine serum albumin from its dimer and other polymeric forms.

Gooding teaches an anion exchange chromatography method where bovine serum albumin is separated from its dimer and other polymeric forms (see page 141; page 143, Figure 3; and page 140) using a buffer containing sodium acetate, 0-1M gradient (see Figure 1 legend) at pH from 6.0 to pH 8.0. Gooding fails to report the yield of the monomeric form of BSA. However, Gagnon teaches that ion exchange chromatography is used to purify proteins and that the mass recovery for monoclonal antibody is 80-95%, with an average of 90% (see page 64). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Gooding to purify the bovine serum albumin monomer from dimers and multimers and one would have expected to have a yield of greater than 90% because of the teachings of Gagnon concerning the general knowledge of the ability of ion exchange chromatography to purify proteins.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,620,918. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of U.S. Patent No. 6,620,918 are narrower in scope than the instant claims (the methods of the 6,620,918 "consist essentially of" ion exchange chromatography, and the yield is 90% with 95% purity), and therefore, are a subspecies that anticipates the instantly claimed methods.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
June 21, 2006

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